## REMARKS

Claims 12-31 are pending in this application. Claims 1-11 have been cancelled without prejudice, and new claims 12-31 have been added. Support for the new claims can be found in the specification at e.g., page 17, line 22, through page 18, line 21; page 23, line 23, through page 24, line 18; page 26, lines 9-14; page 28, lines 9-14; page 36, lines 4-9; page 21, lines 2-11; page 18, line 22, through page 19, line 2; and page 14, lines 19-25. These amendments add no new matter.

35 U.S.C. § 112, Second Paragraph (Indefiniteness)

Claim 5 stands rejected as allegedly indefinite in its use of the term "competitive antigen." On page 2, lines 10-15, of the Office Action, the Examiner states,

> [w]ith respect to claim 5, it is not clear what is meant by 'competitive antigen' in the context of a 'kit.' An 'antigen' is typically used to prepare an antibody and as understood from the specification of the instant application, compound of formula (1) is not used for production of anti-dioxin antibodies. If the 'competitive antigen' is different from the compound of formula (1), then it is unclear what antigen(s) or compound(s)/conjugate are encompassed by the term 'competitive antigen'?

Although claim 5 has been cancelled, and thus its rejection under the present heading has been obviated, newly added claims 12, 13, 17, 18, 22, 23, 27 and 28 also recite the term "competitive antigen" for use in various method steps. Applicants respectfully submit that one of ordinary skill in the art, in reading the instant specification, would understand that the term "competitive antigen" refers to an agent of known concentration and character, that is recognized by the anti-dioxin antibody of the instant methods and is used to measure dioxin concentration in indirect competitive immunoassays. Examples of "competitive antigens" include a dioxin or a complex of a dioxin with carrier protein (see specification, e.g., page 19, lines 15 to 17). As described on page 21, lines 2-11, a "competitive antigen" can also be a chlorophenol derivative of formula (1).

Claims 6-9 stand rejected as allegedly "incomplete for omitting essential steps" and indefinite for not setting forth any steps involved in the method.

Claims 6-9 have been cancelled without prejudice, and thus their rejection under the present heading has been obviated. All of the newly presented method claims set forth active, positive steps (including all essential steps) and satisfy the requirements of 35 U.S.C. § 112, second paragraph.

Claim 10 stands rejected as allegedly indefinite. On page 3, lines 16-20, of the Office Action, the Examiner states that,

> it is unclear how the antigen is detected in the immunoassay method i.e it is not clear whether anti-dioxin antibody is labeled with a detectable label or is detected by secondary labeled antibody. An appropriate method step(s) for the detection of this binding by the use of an appropriate label (tracer) is required to clearly define the method steps.

Claim 10 has been cancelled without prejudice, thereby obviating the present rejection. The methods of new independent claims 12 and 22 include a step of "determining the amount of competitive antigen-antibody complex from a label incorporated into a secondary antibody binding to the primary antibody." Similarly, the methods of new independent claims 17 and 27 include a step of "determining the amount of competitive antigen-antibody complex from a label incorporated into the competitive antigen." Therefore, applicants respectfully submit that new claims 12, 17, 22 and 27 meet the definiteness requirement as specified under 35 U.S.C. § 112, second paragraph.

Claim 10 stands rejected as allegedly indefinite in its use of the phrase "an immunoassay method for dioxins."

Claim 10 has been cancelled without prejudice, thereby obviating the present rejection. New independent claims 12, 17, 22, and 27 clearly set forth the intended uses of the claimed methods.

35 U.S.C. § 102(a) and § 102(b) (Anticipation)

Claims 1-3 stand rejected as allegedly anticipated by each of Hatzidakis et al. (Anal. Chem., 2002, 74:2513-2521; herein referred to as "Hatzidakis"), Feung et al. (J. Arg. Food Chem., 1973, 21(4): 632-637; herein referred to as "Feung"), Japanese Patent Publications 2002-128731, 2002-131316, and 2002-155023, and Carlson et al. (US Patent No. 5,538,852; herein referred to as "Carlson").

Claims 1-3 have been cancelled without prejudice, thereby obviating the present anticipation rejections.

35 U.S.C. § 103(a) (Obviousness)

Claims 6, 7, and 9-11 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Allen et al. (US Published Patent Application No. 2003/0054424; herein referred to as "Allen") in view of Carlson and Hatzidakis.

Claims 6, 7, and 9-11 have been cancelled without prejudice, and thus their rejection has been obviated. Applicants provide the following remarks to address the rejection insofar as it may relate to the methods of new claims 12-31.

The currently claimed methods address the substantial limitations of official (i.e., standardly utilized chromatographic assays) and immunoassays used to quantitate both the concentration and toxic equivalent (TEQ) of dioxin compounds (see specification, for example, page 7, lines 3-5, page 10, lines 2-7). These limitations of prior art assays include, for example:

(1) use of highly toxic reference compounds (e.g., 2,3,7,8-TeCDD) as assay standards (which raise significant safety concerns for the assayer; see specification, for example, page 6, lines 5-10);

(2) use of a reference compound as an assay standard that may be or is a constituent of the analyte sample to be tested (see specification, for example, page 4, lines 15-24, and see (3) below); and

(3) problems in choosing a correct reference compound as an assay standard, since dioxin molecules encompass three different cogeners, each having myriad isomers of different

chlorine substitution patterns and its own unique toxicity. Thus, in choosing one compound as a standard over another the assayer may obtain a TEQ value that is not entirely accurate for a given sample. To achieve high accuracy of dioxin TEQ, traditionally the concentrations of a potential 29 types of dioxins must be measured, and then standardized with their respective TEF values (see specification, for example, page 10, lines 19-24).

The claimed methods address these aforementioned concerns, in part, by use of the compound of formula (1) as a reference compound. First, the toxicity of the compound of formula (1) is expected to be lower than that of dioxin molecules, as it has not been assigned a toxic equivalency by the World Health Organization (WHO), and is derived from the addition of a methylene chain and peptide to a commercially available chlorophenol compound (see specification, for example, page 10, line 25, through page 11, line 7, and page 15, line 11, through page17, line 4). Second, the synthetic compound of formula (1) is not expected to be a natural constituent of any field-obtained analyte samples (e.g., exhaust gas, fly ash, or soil samples), and thus would not inherently detract from the overall accuracy of the assay. Third, the instantly claimed methods provide a facile assay that gives TEQ values highly consistent with traditional, laborious chromatographic techniques, and does not require the assayer to individually measure each dioxin, nor use toxic equivalency factors (TEF) in the TEQ calculation (see specification, for example, page 7, lines 3-18; and page 10, lines 8-24).

Allen, the primary reference cited in the present obviousness rejection, describes an immunoassay method for measuring polychlorinated biphenyl (PCB) compounds. Allen describes using PCB compounds as components of the control composition. However, the control composition of Allen comprises a plurality of PCB compounds that are expected to be present in a sample (see, for example, paragraphs [0039] and [0043] of Allen). Therefore, in using the target compounds as components of the control composition, the methods of Allen are clearly distinct from the claimed methods (that use just one reference compound of formula (1), which is not a constituent of the analyte being tested).

Allen nowhere mentions or suggests that a single, low-toxicity, non-dioxin reference compound be used as a substitute for PCB compounds to address concerns over safety in using

the control composition. Furthermore, in contrast to the claimed methods, not only does the Allen's method fail to alleviate the safety concern of using toxic PCB compounds, but it also requires the assayer to multiply the concentrations of individual PCB compounds present in the sample by their TEFs to calculate their toxicity. There is no mention or suggestion that use of a compound, such as the compound of formula (1), could remedy problems associated with TEQ calculation of different dioxins in a given sample.

Carlson describes a competitive immunoassay for quantitatively determining PCB concentration in a sample. Carlson also discloses chlorophenoxy conjugates with BSA or KHL as competitors, and discloses that such chlorophenoxy conjugates can be used as competitors. However, Carlson nowhere describes or suggests a standard (e.g., the reference compound of formula (1)) that can be used as a substitute for dioxins to prepare a calibration curve. Moreover, Carlson nowhere mentions or even suggests that toxicity of the standard could present safety concerns for the assayer and/or problems in subsequent TEQ calculations.

Hatzidakis describes solutions of phenoxy conjugates, for example, 2,4D and 2,4,5T (i.e., 2,4-dichlorophenoxy acetic acid and 2,4,5-trichlorophenoxy acetic acid). In the passage on page 2517, left column, lines 6-14, Hatzidakis describes mixing a known concentration of 2,4D or 2,4,5T, a tracer and an antibody to prepare a standard curve. However, Hatzidakis performs the above reaction in order to examine which tracer can most effectively improve the detection limit. Furthermore, 2,4D and 2,4,5T are merely used as examples of herbicides present in a sample. Nowhere does Hatzidakis use 2,4D or 2,4,5T or suggest that 2,4D or 2,4,5T can be used for the purpose of preparing a calibration curve.

Applicants respectfully submit that none of the cited references suggest that a compound of formula (1) can be used as a substitute for dioxins to prepare a calibration curve. Moreover, none of the cited references discloses methods of determining the TEQ of dioxins based on a calibration curve using the compound of formula (1) of the instantly claimed methods. Carson and Hatzidakis, neither singly nor in combination, are able to cure the above-described deficiencies in the disclosure of Allen, and thus do not render obvious the methods of new claims 12-31. As a result, applicants respectfully request that the Examiner withdraw the rejection.

Claims 3-5 stand rejected as allegedly unpatentable over Allen, in view of Carlson and Hatzidakis, and in further view of Friedman et al., U.S. Patent No. 5,834,222.

Claims 1-3 have been cancelled without prejudice, thereby obviating the present anticipation rejections.

Double Patenting

Claims 1-5 stand provisionally rejected on the grounds of non-statutory obviousness-type double patenting as allegedly unpatentable over claims 3-6 of co-pending Patent Application No. 10/687,684 (2004/0191846A1).

Claims 1-5 have been cancelled without prejudice, thereby obviating the present non-statutory obviousness-type double patenting rejection.

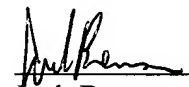
## CONCLUSION

Applicants submit that all grounds for rejection have been overcome and that all claims are in condition for allowance, which action is requested.

Enclosed is a check in payment of excess claim fees. Please apply any additional charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 18900-002US1.

Respectfully submitted,

Date: March 29, 2006



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